Context-dependent effects of Eya1 in sensory neurogenesis

Bahareh Estiri, Gerhard Schlosser

University of Galway, The School of Biological and Chemical Sciences

E-mail: b.estiri1@universityofgalway.ie

Eya1 plays a key role in the development of sensory neurons acting as a cofactor of transcription factor Six1. Previous studies have established a context-dependent role of the Eya1/Six1 complex in cranial sensory neurogenesis with high levels promoting proliferation and low levels promoting neuronal differentiation. The main goal of this study is to clarify how Eya1 exerts its context-specific functions in progenitor cells versus differentiated sensory neurons. In a first step, we are currently identifying the target genes of Eya1 specific for progenitors and differentiating sensory neurons using RNA-Seq. We use specific promoter-GFP constructs (e.g., with promoters for sox3 and NTubulin) to selectively drive GFP expression in either progenitors or differentiated sensory neurons of Xenopus laevis embryos. Promoter-GFP constructs are generated by pTransgenesis and are integrated into the genome using I-SceI meganuclease. Overexpression of Eya1 in embryos transgenic for the different promoter-GFP constructs followed by FACS-sorting of GFP-positive cells and RNA sequencing allows us to specifically identify Eya1 target genes in progenitor cells versus differentiating neurons. In a second step, we will further characterize these target genes in gain and loss of function studies. This approach will help us to elucidate the context-specific role of Eya1 in progenitors and differentiating neurons during the development of sensory organs. Our study also promises new insights into the etiology of sensorineural disorders in human patients after mutations in Eya1 (e.g., Branchiootorenal syndrome).

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